Scientific Opinion on the application (EFSA-GMO-BE-2012-110) for the placing on the market of tissue-selective herbicide-tolerant genetically modified maize MON 87427 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto

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Abstract: Maize MON 87427 was developed by Agrobacterium tumefaciens-mediated transformation to express the CP4 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS) protein, in all tissues except for the male reproductive tissues, conferring tissue-selective tolerance to glyphosate. The molecular characterisation of maize MON 87427 did not give rise to safety issues. Agronomic and phenotypic characteristics as well as compositional data of maize MON 87427 did not raise food/feed and environmental safety concerns. No differences in the compositional data requiring further safety assessment were identified. There were no concerns regarding the potential toxicity and allergenicity of the newly expressed CP4 EPSPS protein. The nutritional value of maize MON 87427 is not expected to differ from that of non-genetically modified (GM) maize varieties. There are no indications of an increased likelihood of establishment or spread of feral maize plants. Given its intended use in food and feed, interactions with the biotic and abiotic environment were not considered an issue. Risks associated with an unlikely, but theoretically possible, horizontal gene transfer from maize MON 87427 to bacteria have not been identified. The monitoring plan and reporting intervals are in line with the scope of the application for maize MON 87427. In conclusion, the EFSA Panel on Genetically Modified Organisms considers that the information available for maize MON 87427 addresses the scientific comments raised by Member States and that the maize MON 87427, as described in this application, is as safe as its conventional counterpart and non-GM reference varieties with respect to potential effects on human and animal health and the environment in the context of the scope of the application.

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SCIENTIFIC OPINION

Scientific Opinion on the application (EFSA-GMO-BE-2012-110) for the placing on the market of tissue-selective herbicide-tolerant genetically modified maize MON 87427 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto[1]

EFSA Panel on Genetically Modified Organisms (GMO)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Maize MON 87427 was developed by *Agrobacterium tumefaciens*-mediated transformation to express the CP4 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS) protein, in all tissues except for the male reproductive tissues, conferring tissue-selective tolerance to glyphosate. The molecular characterisation of maize MON 87427 did not give rise to safety issues. Agronomic and phenotypic characteristics as well as compositional data of maize MON 87427 did not raise food/feed and environmental safety concerns. No differences in the compositional data requiring further safety assessment were identified. There were no concerns regarding the potential toxicity and allergenicity of the newly expressed CP4 EPSPS protein. The nutritional value of maize MON 87427 is not expected to differ from that of non-genetically modified (GM) maize varieties. There are no indications of an increased likelihood of establishment or spread of feral maize plants. Given its intended use in food and feed, interactions with the biotic and abiotic environment were not considered an issue. Risks associated with an unlikely, but theoretically possible, horizontal gene transfer from maize MON 87427 to bacteria have not been identified. The monitoring plan and reporting intervals are in line with the scope of the application for maize MON 87427. In conclusion, the EFSA Panel on Genetically Modified Organisms considers that the information available for maize MON 87427 addresses the scientific comments raised by Member States and that the maize MON 87427, as described in this application, is as safe as its conventional counterpart and non-GM reference varieties with respect to potential effects on human and animal health and the environment in the context of the scope of the application.

KEY WORDS

GMO, maize (*Zea mays*), MON 87427, tissue-selective, herbicide tolerance, CP4 EPSPS, Regulation (EC) No. 1829/2003

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[1] On request from the Competent Authority of Belgium, Question No EFSA-Q-2012-00692, adopted on 27 May 2015.

[2] Panel members: Salvatore Arpaia, Andrew Nicholas Edmund Birch, Andrew Chesson, Patrick du Jardin, Achim Gathmann, Jürgen Gropp, Lieve Herman, Hilde-Gunn Hoen-Sorteberg, Huw Jones, József Kiss, Gijs Kleter, Martinus Løvik, Antoine Messéan, Hanspeter Naegeli, Kaare Magne Nielsen, Jaroslava Ovesná, Joe Perry, Nils Rostoks and Christoph Tebbe. Correspondence: gmo@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank the members of the Working Groups on Molecular Characterisation, Food and Feed Safety Assessment and on Environmental Risk Assessment for the preparatory work on this scientific opinion and the EFSA staff Hermann Broll, Zoltán Divéki and Andrea Gennaro for the support provided to this scientific opinion.

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SUMMARY

Following the submission of an application (EFSA-GMO-BE-2012-110) under Regulation (EC) No 1829/2003 by Monsanto, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) was asked to deliver a scientific opinion on the safety of tissue-selective herbicide-tolerant genetically modified (GM) maize (*Zea mays* L.) MON 87427 (Unique Identifier MON-87427-7). The scope of application EFSA-GMO-BE-2012-110 is for import, processing, and food and feed uses of maize MON 87427 within the European Union (EU) in the same way as any non-GM maize, but excludes cultivation in the EU.

The EFSA GMO Panel evaluated maize MON 87427 with reference to the scope and appropriate principles described in its guidelines for the risk assessment of GM plants and derived food and feed, the environmental risk assessment of GM plants and the post-market environmental monitoring of GM plants. The scientific evaluation of the risk assessment included molecular characterisation of the inserted DNA and analysis of the expression of the corresponding protein. An evaluation of the comparative analyses of compositional, agronomic and phenotypic characteristics was undertaken, and the safety of the newly expressed proteins and the whole food/feed was evaluated with respect to potential toxicity, allergenicity and nutritional wholesomeness. An evaluation of environmental impacts and the post-market environmental monitoring plan was also undertaken.

Maize MON 87427 was developed by *Agrobacterium tumefaciens*-mediated transformation of immature maize embryos. The resulting GM maize expresses 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS) from *Agrobacterium* sp. strain CP4, which confers tolerance to the herbicidal active substance glyphosate. However, CP4 EPSPS expression is absent or limited in male reproductive tissues, which eliminates or reduces the need for detasseling when MON 87427 is used as a female parent in hybrid maize seed production. The molecular characterisation data established that maize MON 87427 contains a single insert consisting of the CP4 *epsps* expression cassette. No other parts of the plasmid used for transformation were detected in maize MON 87427. Bioinformatics analyses and genetic stability studies did not give rise to any safety issues. The levels of the CP4 EPSPS protein in maize MON 87427 were determined and reported adequately.

Based on the agronomic and phenotypic characteristics of maize MON 87427 under the tested conditions (treated and not treated with the intended herbicide), some differences were observed in maize MON 87427 compared with its conventional counterpart. The EFSA GMO Panel concluded that none of the differences identified in the composition, agronomic and phenotypic characteristics of grain and forage obtained from maize MON 87427 is relevant to food and feed safety.

No concerns regarding the potential toxicity or allergenicity of the newly expressed CP4 EPSPS protein were identified, and no evidence that the genetic modification might significantly change the overall allergenicity of maize MON 87427 was found. The nutritional value of food and feed derived from maize MON 87427 is not expected to differ from that of food and feed derived from non-GM maize varieties. The EFSA GMO Panel concludes that maize MON 87427 assessed in this application is as safe and nutritious as its conventional counterpart and the commercial non-GM maize varieties tested.

Application EFSA-GMO-BE-2012-110 covers the import, processing, and food and feed uses of maize MON 87427, and excludes cultivation. Therefore, there is no requirement for a scientific assessment of possible environmental effects associated with the cultivation of this GM maize. The EFSA GMO Panel concluded that there are no indications of an increased likelihood of establishment or spread of feral maize MON 87427 plants in the event of the accidental release of viable GM maize grains into the environment. Potential interactions with the biotic and abiotic environment were not considered an issue by the EFSA GMO Panel. Risks associated with an unlikely, but theoretically possible, horizontal gene transfer from maize MON 87427 to bacteria have not been identified. The scope of the post-market environmental monitoring plan provided by the applicant is in line with the scope of the maize MON 87427 application and the guidance document of the EFSA GMO Panel on

post-market environmental monitoring of GM plants (EFSA, 2011a). The EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in the monitoring plan.

In delivering its scientific opinion, the EFSA GMO Panel took into account application EFSA-GMO-BE-2012-110, additional information provided by the applicant, scientific comments submitted by the Member States and relevant scientific publications. In conclusion, the EFSA Panel on Genetically Modified Organisms considers that the information available for maize MON 87427 addresses the scientific comments raised by Member States and that the maize MON 87427, as described in this application, is as safe as its conventional counterpart and non-GM reference varieties with respect to potential effects on human and animal health and the environment in the context of the scope of the application.

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1. Introduction

Maize MON 87427 was developed to confer tissue-selective tolerance to glyphosate-based herbicides[4]. The tolerance does not extend to male reproductive cells, such as microspores and tapetum cells; therefore, two properly timed glyphosate applications (at vegetative growth stages from V8 to V13) will produce male sterile phenotype plants. This significantly reduces or eliminates the need for detasseling of female inbred lines, an agronomic practice currently used in hybrid maize seed production. Tissue-specific tolerance to glyphosate (*N*-(phosphonomethyl)glycine) was achieved by the expression of CP4 5-enolpyruvylshikimate-3-phosphate synthase (CP4 EPSPS) under the control of a specific promoter and intron combination (see Section 3.1.1.1). CP4 EPSPS has a reduced affinity for glyphosate; therefore, glyphosate spraying does not interrupt the biosynthesis of essential amino acids in maize MON 87427.

1.1. Background

On 21 June 2012, the European Food Safety Authority (EFSA) received from the Belgian Competent Authority an application (Reference EFSA-GMO-BE-2012-110) for authorisation of GM maize MON 87427 (Unique Identifier MON-87427-7), submitted by Monsanto within the framework of Regulation (EC) No 1829/2003 on GM food and feed[5].

After receiving the application EFSA-GMO-BE-2012-110, and in accordance with Articles 5(2)(b) and 17(2)(b) of the Regulation (EC) No 1829/2003, EFSA informed the Member States and the European Commission, and made the summary of the application publicly available on the EFSA website[6]. EFSA initiated a formal review of the application to check compliance with the requirements laid down in Articles 5(3) and 17(3) of the Regulation (EC) No 1829/2003. On 9 October 2012 and 28 November 2012, EFSA received additional information requested under completeness check (on 12 September 2012 and 30 October 2012, respectively). On 3 January 2013, EFSA declared the application as valid in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003.

EFSA made the valid application available to Member States and the European Commission, and consulted nominated risk assessment bodies of Member States, including national Competent Authorities within the meaning of Directive 2001/18/EC[7] following the requirements of Articles 6(4) and 18(4) of Regulation (EC) No 1829/2003, to request their scientific opinion. Member States had three months after the date of receipt of the valid application (until 3 April 2013) to make their opinion known.

On 11 April 2013, 3 June 2013, 13 August 2013, 6 June 2014 and 15 December 2014, 16 March 2015 and on 7 May 2015 the EFSA GMO Panel requested additional information from the applicant. The applicant provided the requested information on 17 June 2013, 11 September 2013, 13 December 2013, 8 July 2014, 2 March 2015, 13 April 2015, 20 April 2015 and on 8 May 2015. The applicant also spontaneously provided additional information on 5 December 2013.

In giving its scientific opinion on maize MON 87427 to the European Commission, Member States and the applicant, and in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003, EFSA has endeavoured to respect a time limit of six months from the acknowledgement of the valid application. As additional information was requested by the EFSA GMO Panel, the time limit of six months was extended accordingly, in line with Articles 6(1), 6(2), 18(1), and 18(2) of Regulation (EC) No 1829/2003.

[4] Dossier: Part II—Section A.2.2.1.

[5] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. OJ L 268, 18.10.2003, p. 1–23.

[6] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2012-00692

[7] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. OJ L 106, 12.3.2001, p. 1–38.

According to Regulation (EC) No 1829/2003, this scientific opinion is to be seen as the report requested under Articles 6(6) and 18(6) of that Regulation and thus will be part of the EFSA overall opinion in accordance with Articles 6(5) and 18(5).

1.2. Terms of Reference as provided by requestor

The EFSA GMO Panel was requested to carry out a scientific assessment of maize MON 87427 for food and feed uses, import and processing in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003.

Where applicable, any conditions or restrictions which should be imposed on the placing on the market and/or specific conditions or restrictions for use and handling, including post-market monitoring requirements based on the outcome of the risk assessment and, in the case of GMOs or food/feed containing or consisting of GMOs, conditions for the protection of particular ecosystems/environment and/or geographical areas should be indicated in accordance with Articles 6(5)(e) and 18(5)(e) of Regulation (EC) No 1829/2003.

The EFSA GMO Panel was not requested to give an opinion on information required under Annex II to the Cartagena Protocol. Furthermore, the EFSA GMO Panel did not consider proposals for labelling and methods of detection (including sampling and the identification of the specific transformation event in the food/feed and/or food/feed produced from it), which are matters related to risk management.

2. Data and Methodologies

2.1. Data

In delivering its scientific opinion, the EFSA Panel on Genetically Modified Organisms (EFSA GMO Panel) took into account application EFSA-GMO-BE-2012-110, additional information provided by the applicant, scientific comments submitted by the Member States and relevant scientific publications.

2.2. Methodologies

The EFSA GMO Panel carried out an evaluation of the scientific risk assessment of maize MON 87427 for food and feed uses, import and processing in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003. The EFSA GMO Panel took into account the appropriate principles described in its guidelines for the risk assessment of GM plants and derived food and feed (EFSA GMO Panel, 2011b), for the environmental risk assessment of GM plants (EFSA GMO Panel, 2010a) and for the post-market environmental monitoring (PMEM) of GM plants (EFSA GMO Panel, 2011a).

The comments raised by Member States are addressed in Annex G of EFSA's overall opinion[8], and were taken into consideration during the evaluation of the risk assessment.

3. Assessment

3.1. Molecular characterisation

3.1.1. Evaluation of relevant scientific data

3.1.1.1. Transformation process and vector constructs

Maize MON 87427 was developed by *Agrobacterium tumefaciens* (also known as *Rhizobium radiobacter*)-mediated transformation. Immature maize (*Zea mays* L., line LH198 × HiII) embryos

[8] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2012-00692

were co-cultured with the *A. tumefaciens* strain ABI containing the transformation binary plasmid PV-ZMAP1043[9].

The PV-ZMAP1043 vector contains a single expression cassette consisting of the following transfer DNA (T-DNA): an enhanced 35S promoter from the *Cauliflower mosaic virus*; the *hsp70* intron derived from the maize heat shock protein 70 gene; the chloroplast-targeting sequence from the *Arabidopsis thaliana shkG* gene (encoding the EPSPS protein); the codon-optimised coding sequence of the *aro*A gene from *Agrobacterium* sp. strain CP4 (encoding the CP4 EPSPS protein)[10]; and the 3′-untranslated region from the *A. tumefaciens* nopaline synthase (*nos*) gene (T-*nos*), which terminates transcription[11]. In addition to these genetic elements, the PV-ZMAP1043 vector also contains the left- and right-border sequences from *A. tumefaciens*, which are used for the transfer of the T-DNA to the plant cells.

The vector backbone sequence contains the bacterial *aad*A gene from *Escherichia coli* transposon Tn*7*, which confers resistance to streptomycin and spectinomycin, the origin of replication from the pBR322 plasmid, the *rop* coding sequence from the ColE1 plasmid, and the origin of replication from the broad host range plasmid RK2.

3.1.1.2. Transgene constructs in the genetically modified plant

The molecular characterisation of maize MON 87427 was performed using Southern analysis, polymerase chain reactions (PCRs) and DNA sequence analysis, in order to determine copy number, size and organisation of the inserted sequences, and to confirm the absence of plasmid backbone sequences[12]. The approach used was acceptable, in terms of both coverage and sensitivity.

Southern analyses indicated that maize MON 87427 contains a single insert, which consists of a single copy of the T-DNA in the same configuration as in the PV-ZMAP1043 transformation vector. The insert and copy number were confirmed by the hybridisation signals generated by digestion with the restriction enzymes *Nco*I and *Nsi*I, together with four probes covering the T-DNA region. The absence of vector backbone sequences was tested by Southern analysis, after *Nco*I and *Nsi*I restriction digestion, with three backbone-specific overlapping probes.

The insert and the 5′- and 3′-flanking regions of maize MON 87427 were sequenced. The results were in line with those obtained using Southern analyses. The insert of 3 681 bp is identical to the corresponding region of PV-ZMAP1043. Comparison of the flanking regions with the wild type pre-insertion locus revealed that, during the T-DNA integration, 140 bp were deleted, 41 bp were inserted upstream of the MON 87427 insert and 24 bp were inserted downstream of the insert[13]. The possible interruption of known endogenous maize genes in MON 87427 was evaluated by bioinformatic analyses of the pre-insertion locus and of the genomic sequences flanking the insert[14]. Analysis of the 703 bp upstream of the 5′-flanking region of the insert revealed close similarity to various maize expressed sequence tag (EST) clones. However, extended bioinformatic searches did not reveal any know function of this genomic region and there are no indications from comparative phenotypic, agronomic or compositional analyses of any unintended effect caused by the insertion (see Sections 3.2, 3.3 and 3.4). The results of segregation and bioinformatic analyses established that the insert is located in the nuclear genome[15].

[9] Dossier: Part II—Section A.2.1.1.
[10] The CP4 EPSPS protein resulting from the translation of the *Agrobacterium* sp. strain CP4 *aro*A coding sequence has already been evaluated by EFSA in the context of the following applications: EFSA-GMO-RX-MON1445, EFSA-GMO-UK-2004-08, EFSA-GMO-NL-2005-22, EFSA-GMO-NL-2005-24, EFSA-GMO-CZ-2005-27, EFSA-GMO-NL-2006-36, EFSA-GMO-UK-2007-41, EFSA-GMO-NL-2010-78, EFSA-GMO-NL-2010-87, EFSA-GMO-BE-2011-101.
[11] Dossier: Part II—Section A.2.1.2.
[12] Dossier: Part II—Section A.2.2.2.
[13] Dossier: Part II—Section A.2.2.2.ii.
[14] Dossier: Part II—Section A.2.2.2.v.
[15] Dossier: Part II—Section A.2.2.2.iv.

In order to assess whether the sequences encoding the newly expressed proteins or any other open reading frames (ORFs) present within the insert and spanning the junction sites raise any safety issue, their *in silico* translation products were compared for similarities with known allergens and toxins by using suitable algorithms and appropriate databases[16]. In addition, the presence of eight amino acid perfect matches between the known allergens of the database and the *in silico* translation products was examined. Bioinformatic analysis revealed no biologically relevant similarities to allergens or toxins for the newly expressed protein or any of the putative peptides that might be produced from ORFs within the insert or spanning the junction regions. These bioinformatic analyses support the conclusion that, even in the unlikely event that any of the new ORFs at the junctions were translated, they would not raise a safety issue.

In order to conclude on the possibility of horizontal gene transfer by homologous recombination (HR), the applicant performed a sequence identity analysis of the regions of bacterial origin in maize MON 87427. Four elements were identified: the truncated left border, the CP4 EPSPS-coding sequence, the T-*nos* terminator and the right border. Among these regions, two have sufficient length and identity to support HR (de Vries and Wackernagel, 2002; Monier et al., 2007; Hülter and Wackernagel, 2008; EFSA, 2009a; Overballe-Petersen et al., 2013), namely the 251 bp fragment of the tumour-inducing (Ti-)plasmid of *A. tumefaciens* Ti T37 containing the left border region used for transfer of the T-DNA, and the T-*nos* terminator isolated from *A. tumefaciens* Ti 15955.

As indicated, the left border fragment and the T-*nos* terminator could support HR but these were isolated from different *A. tumefaciens* plasmids (Ti T37 is an octopine plasmid and Ti 15955 is a nopaline plasmid). The applicant, in the analysis provided, did not identify a single plasmid that contained both the left border and the T-*nos* terminator. A single alignment with the same *A. tumefaciens* Ti-plasmid sequence of sufficient length and identity to support HR (EFSA, 2009a) was identified. As a result, there is no indication for a possible double HR with the Ti-plasmid of *A. tumefaciens*.

Neither the codon-optimised CP4 *epsps* gene, which shares 84 % sequence identity with the native prokaryotic sequence, nor the 35 bp-long right border would trigger further considerations of HR-facilitated gene transfer.

The likelihood and potential consequences of plant-to-bacteria gene transfer are described in Section 3.4.1.1.

3.1.1.3. Information on the expression of the insert

The levels of the CP4 EPSPS protein in forage and grain from maize MON 87427 were analysed by enzyme-linked immunosorbent assay (ELISA) in samples collected from five field trials conducted in the USA during 2010. The trials were performed within the major maize-growing regions of the USA under a variety of environmental conditions. The samples analysed included both those treated with and those not treated with glyphosate[17]. Considering the scope of the application, the CP4 EPSPS protein levels in grain and forage are considered the most relevant (Table 1) although only grain is subject to importation.

Table 1: CP4 EPSPS levels (µg/g dry weight), expressed as mean ± standard deviation and range in brackets, in grain and forage from maize MON 87427 (n = 18)

Tissue	Glyphoste treatment	
	Untreated	Treated
Grain	5.6 ± 0.89 (4.1–6.9)	4.9 ± 1.2 (2.7–7.1)
Forage	75 ± 27 (35–130)	140 ± 57 (62–270)

[16] Dossier: Part II—Section A.2.2.2.(v); additional information: 20/04/2015.
[17] Dossier: Part II—Section A.2.2.3.

3.1.1.4. Inheritance and stability of inserted DNA

Genetic stability of the insert in MON 87427 was assessed by Southern analysis of genomic DNA from five generations. The restriction enzyme/probe combination used provided sufficient evidence to conclude that the tested plants retained a single copy of the insert and its flanking regions, which were stably inherited in subsequent generations[18].

Phenotypic stability was observed by segregation analysis of the herbicide tolerance trait in plants from three generations of maize MON 87427. The results supported the presence of a single insertion, segregating in a Mendelian fashion.

3.1.2. Conclusions on molecular characterisation

The molecular characterisation data establish that maize MON 87427 contains a single insert consisting of one copy of the CP4 *epsps* expression cassette. Bioinformatic analyses of the newly expressed protein and the ORFs spanning the junction sites within the insert or between the insert and genomic DNA did not give rise to safety issues. Bioinformatic analyses also indicated that the potential for double HR with bacterial DNA was very low. The stability of the inserted DNA and of the introduced herbicide tolerance trait was confirmed over several generations.

3.2. Comparative analysis

3.2.1. Evaluation of relevant scientific data

3.2.1.1. Choice of comparator and production of material for the comparative assessment[19]

Application EFSA-GMO-BE-2012-110 presents data on agronomic and phenotypic characteristics, as well as on the seed and forage composition of maize MON 87427, its conventional counterpart (HCL301 × LH287)[20] and a set of non-GM maize reference varieties harvested from field trials performed at eight locations in the USA in 2010[21]. Maize MON 87427 back-crossed six times into the genetic background HCL301 and maize line HCL301 (to become a conventional counterpart) were crossed with inbred line LH287 to produce the GM and comparator hybrids to be grown in the field trials. All field trial sites were in areas where maize is typically cultivated in the USA. At each site, the following maize materials were grown in a randomised complete block design with four replicates: maize MON 87427, the conventional counterpart and four different non-GM maize reference varieties, all treated with required maintenance pesticides; and maize MON 87427 treated with glyphosate and required maintenance pesticides. Overall, the field trials included 25 non-GM maize reference varieties[22] in order to estimate the natural variation in composition and agronomic/phenotypic characteristics. The applicant justified the exclusion of one of the original sites from the compositional analysis because of non-compliance with internal quality criteria for pollen sample collection. As a substitute for this site, the applicant provided compositional data from another location.

Seed germination (of F_2 seeds) and pollen morphology and viability were evaluated under laboratory (growth chamber) conditions; however, in this case, event MON 87427 was in the LH198 genetic background[23]. Therefore, for these studies, maize hybrid LH198 × LH287 was used as a comparator.

[18] Dossier: Part II—Section A.2.2.4.
[19] Dossier: Part II—Sections A.3.1 and A.3.2; additional information: 11/09/2013, 08/07/2014, 02/03/2015 and 08/05/2015.
[20] Maize HCL301 × LH287 and maize MON 87427 shared the same breeding scheme, see Technical dossier/Figure 5.
[21] The field trials were located in Jackson County, Arkansas (ARNE), Greene County, Iowa (IABG), Jefferson County, Iowa (IARL) (only for compositional data), Clinton County, Illinois (ILCY), Stark County, Illinois (ILWY), Boon County, Indiana (INFK), Pawnee County, Kansas (KSLA), Miami County, Ohio (OHTR) (only for agronomic and phenotypic data), and York County, Nebraska (NEYO).
[22] The non-GM reference materials were Burrus 645, Maizebelt × 6043, DKC60-15, DKC61-50, Fielder's Choice NG6778, Fontanelle 4924, H-9180, iMaize 110.M7, Legacy L6600, Legacy L6673, Lewis 7007, Midland Phillips 799, Midland Phillips 7B15P, Midwest Genetics 78130, Mycogen 2M746, NK N64Z, NC+ 5411, NK N72-G8, Pioneer 32B81, Pioneer 32T16, Pioneer 33T56, Specialty 4672A, Stewart S518, Stewart S588 and Triumph 1416.
[23] Produced by crossing maize MON 87427 (in LH287 genetic background) with maize LH198 and back-crossing the established hybrids with LH198 three times.

The EFSA GMO Panel considers that LH198 × LH287 has a genetic background comparable to that of the tested MON 87427 line used in the studies conducted under controlled conditions, as documented by the pedigree, and is regarded as an appropriate conventional counterpart.

3.2.1.2. Statistical analysis of field trials data

The applicant performed the comparative assessment using statistical methodology recommended by the EFSA GMO Panel (2010b, 2011b). This recommends the simultaneous application of a test of difference, to determine whether or not the GM plant is different from its conventional counterpart, and a test of equivalence, to determine whether or not the GM plant falls within the natural variation estimated from the non-GM maize reference varieties included in the study. In accordance with the 2011 EFSA guidance (EFSA GMO Panel, 2011b), the result of the equivalence test was categorised into four possible outcomes to facilitate the drawing of conclusions with respect to the presence or absence of equivalence: category I indicates full equivalence; category II indicates that equivalence is more likely than non-equivalence; category III indicates that non-equivalence is more likely than equivalence; and category IV indicates non-equivalence.

3.2.1.3. Agronomic and phenotypic characteristics[24]

Agronomic and phenotypic characteristics tested under field conditions

Fourteen endpoints were measured in the agronomic and phenotypic field trials: early vigour, early stand count, days to 50 % pollen shed, days to 50 % silking, stay green rating, ear height, plant height, dropped ear count, stalk lodged plants, root lodged plants, final stand count, grain moisture, test weight and yield. Visually observable responses to naturally occurring diseases, abiotic stress and arthropod damage were also recorded in order to provide indications of altered stress responses of maize MON 87427 as compared with its conventional counterpart.

Statistically significant differences between maize MON 87427 and its conventional counterpart (HCL301 × LH287), both treated with required maintenance pesticides only, were observed for five endpoints: days to 50 % pollen shed, ear height, plant height, early stand count and grain moisture. For one of these significantly different endpoints, plant height, a significant genotype–environment interaction was identified but no consistent relationship with descriptive site characteristics was observed.

Statistically significant differences between maize MON 87427 treated with glyphosate and its conventional counterpart (HCL301 × LH287) were observed for three endpoints: days to 50 % pollen shed, ear height and plant height.

All of the significantly different agronomic and phenotypic characteristics of maize MON 87427 (both treated with required maintenance pesticides only and additionally treated with glyphosate) were demonstrated to be equivalent to the corresponding characteristics of the non-GM maize reference varieties (equivalence category I). Given the nature of these endpoints and the outcomes of the statistical analyses, no further assessment of the significant differences observed was considered necessary with respect to food and feed safety.

Also, no altered stress responses of maize MON 87427, compared with its conventional counterpart, with regard to visually observable responses to naturally occurring diseases, abiotic stress and arthropod damage were observed.

Agronomic and phenotypic characteristics tested under controlled conditions

(a) Pollen characteristics[25]

[24] Dossier: Part II—Section A.3.4; additional information: 17/06/2013, 11/09/2013, 08/07/2014, 02/03/2015 and 08/05/2015.
[25] Dossier: Part II—Section A.3.4.

The applicant also reported data on the pollen characteristics of maize MON 87427. Pollen morphology and viability from maize MON 87427, its conventional counterpart (LH198 × LH287) and three non-GM maize reference varieties were measured. Pollen was obtained from plants grown in the open field. The parameters analysed were pollen viability, diameter and general morphology. The applicant observed no significant differences between maize MON 87427 and its conventional counterpart for pollen diameter and general morphology. MON 87427 was found to have significantly higher viability than the control. The difference between maize MON 87427 and its conventional counterpart for pollen viability was less than 1 percentage point, and is not biologically meaningful.

Owing to the insensitivity of the Alexander's stain technique to measure pollen viability, the EFSA GMO Panel considers that the data on pollen viability is inappropriate for the comparative assessment. Alexander's stain is a preliminary test assessing pollen grain maturity, but does not directly measure pollen viability or germination capacity (Dafni, 1992).

(b) Seed characteristics

The applicant also reported data on maize MON 87427 seed characteristics. Seed germination tests with seeds harvested from maize MON 87427 (F_2), its conventional counterpart (LH198 × LH287), and seven non-GM maize varieties, grown under field conditions in two of the tested sites in 2010, were performed to evaluate seed characteristics under growth chamber conditions. Seeds were incubated in growth chambers under controlled conditions at different temperatures. The endpoints analysed were the numbers of normal germinated seeds, abnormal germinated seeds, hard seeds, dead seeds and firm swollen seeds. The applicant found no statistically significant differences between maize MON 87427 and its conventional counterpart.

Although the applicant refers to seed dormancy when discussing the generated data on maize MON 87427 seed characteristics, no data on induced seed dormancy were supplied. Therefore, the EFSA GMO Panel considers that only the conclusions on seed germination of maize MON 87427 are substantiated by the provided data.

As indicated above, the specific studies on pollen viability and seed dormancy supplied by the applicant, in support of the comparative assessment of maize MON 87427, are not considered suitable by the EFSA GMO Panel. However, given that the genetic modification of maize MON 87427 is not designed to target specific pollen and seed characteristics, that maize is not a persistent and invasive crop, and that the scope of the application with regard to maize MON 87427 excludes cultivation, the EFSA GMO Panel considers that data on pollen viability and seed dormancy are not essential for the risk assessment of maize MON 87427.

3.2.1.4. Compositional analysis[26]

The spectrum of compositional parameters measured in maize seeds and forage followed OECD recommendations (OECD, 2002). In total, 63 parameters were analysed: 54 for seeds[27] and nine for

[26] Dossier: Part II—Section A.3.3; additional information: 11/09/2013.

[27] Proximates (ash, carbohydrates by calculation, total fat, moisture and protein), fibres (acid detergent fibre, neutral detergent fibre and total dietary fibre), amino acids (alanine, arginine, aspartic acid, cystine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine), fatty acids (palmitic acid (16:0), palmitoleic (16:1), stearic acid (18:0), oleic acid (18:1), linoleic acid (18:2), linolenic acid (18:3), arachidic acid (20:0), eicosenoic acid (20:1) and behenic acid (22:0)), minerals (calcium, copper, iron, magnesium, manganese, phosphorus, potassium and zinc), vitamins (folic acid, vitamin A (beta-carotene), vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B3 (niacin), vitamin B6 (pyridoxine) and vitamin E (alpha-tocopherol)), anti-nutrients (phytic acid and raffinose) and secondary metabolites (ferulic acid and *p*-coumaric acid).

forage[28]. Fifteen parameters, having more than 50 % of observations below the limit of quantification, were excluded from the statistical analysis[29].

The test of difference for samples sprayed with only maintenance pesticides identified statistically significant differences between maize MON 87427 and its conventional counterpart for seven seed parameters[30], and for two forage parameters (moisture and acid detergent fibre (ADF)). The test of equivalence indicated that all of the significantly different parameters, except one, fell within the equivalence limits (equivalence categories I and II) established from the non-GM maize reference varieties. The test of equivalence could not be performed on ADF in forage because of the small variation among the non-GM reference varieties.

The test of difference between compositional endpoints of maize for samples of MON 87427 sprayed with glyphosate in addition to required maintenance pesticides and the corresponding endpoints of the conventional counterpart sprayed with only required maintenance pesticides identified significant differences for 22 seed parameters[31]. No significant differences were identified with regard to forage. The test of equivalence indicated that all of the significantly different endpoints fell within the equivalence limits (equivalence categories I and II) established from the non-GM maize reference varieties. For 13 of the 22 significantly different endpoints[32], a significant genotype–environment interaction was identified. The compositional data on maize MON 87427 sprayed with glyphosate from this field trial have been published; however, the results in this publication were analysed using an alternative statistical methodology (Venkatesh et al., 2014).

The EFSA GMO Panel assessed all compositional differences between maize MON 87427 and its conventional counterpart. After considering the well-known chemical characteristics of the compounds concerned, and the magnitudes of the changes observed, the EFSA GMO Panel did not identify any difference which requires further assessment with regard to food and feed safety. For each of the parameters for which a significant genotype–environment interaction was detected, no consistent relationship with descriptive site characteristics was observed.

3.2.2. Conclusions on comparative analysis

Based on the agronomic and phenotypic characteristics of maize MON 87427 tested under field conditions, some differences were found between maize MON 87427 and its conventional counterpart. The implications for environmental safety are addressed in Section 3.4.

The EFSA GMO Panel concluded that none of the differences identified in the composition, agronomic and phenotypic characteristics of grain and forage obtained from maize MON 87427 required further assessment regarding food and feed safety.

[28] Protein, total fat, moisture, ash, NDF, ADF, calcium, phosphorus and carbohydrates by calculation.

[29] These were caprylic acid (8:0), capric acid (10:0), lauric acid (12:0), myristic acid (14:0), myristoleic acid (14:1), pentadecanoic acid (15:0), pentadecenoic acid (15:1), heptadecanoic acid (17:0), heptadecenoic acid (17:1), gamma-linolenic acid (18:3), eicosadienoic acid (20:2), eicosatrienoic acid (20:3), arachidonic acid (20:4), sodium and furfural.

[30] The amino acid cystine, the fatty acids palmitic acid (16:0) and linolenic acid (18:3), vitamin B6, TDF, zinc and the secondary metabolite *p*-coumaric acid.

[31] Ash, the amino acids alanine, cysteine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine and tyrosine, the fatty acids palmitic acid (16:0), oleic acid (18:1) and linolenic acid (18:3), vitamin B6, phytic acid, TDF, potassium and copper.

[32] Ash, alanine, cystine, glutamic acid, isoleucine, leucine, phenylalanine, serine, threonine, tyrosine, palmitic acid (16:0), linolenic acid (18:3) and potassium.

3.3. Food/feed safety assessment

3.3.1. Evaluation of relevant scientific data

3.3.1.1. Effects of processing[33]

Maize MON 87427 is intended to be used for production and manufacturing of food and feed products, as are other commercial maize varieties. Taking into account the compositional analysis, which provides no indication of biologically relevant compositional changes except that maize MON 87427 expresses the CP4 EPSPS protein, the EFSA GMO Panel has no reason to assume that the characteristics of maize MON 87427 and derived processed products would be different from those of the products derived from conventional maize varieties, except for the presence of the CP4 EPSPS protein.

3.3.1.2. Toxicology

(a) Toxicological assessment of the newly expressed protein[34]

The EFSA GMO Panel has previously assessed the CP4 EPSPS protein in the context of several applications for the placing on the EU market of GM maize (EFSA, 2009b, c) and other GM crops (EFSA, 2006, 2008; EFSA GMO Panel, 2011c, 2012a, b, 2013a, b, 2014) and did not identified safety concerns. The EFSA GMO Panel is of the opinion that no scientific data have emerged which call for a change of this opinion[35].

Bioinformatics[36]

Updated bioinformatic analysis of the amino acid sequence of the CP4 EPSPS protein revealed no significant similarities to known toxic proteins.

(b) Toxicological assessment of new constituents other than proteins[37]

The outcome of the molecular characterisation and the comparative analysis of maize MON 87427 did not identify issues requiring further toxicological assessment.

3.3.1.3. Animal studies with the food/feed derived from GM plants

Sub-chronic toxicity study in rodents[38]

The applicant provided a sub-chronic (90-day) toxicity study using a protocol which was adapted from OECD TG 408 (OECD, 2008). Five groups of Crl:CD(SD) rats (12 males and 12 females per group), individually housed, were fed diets containing grain from maize MON 87427 (sprayed with the intended herbicide), from a near isogenic non-GM comparator (control), or from one of three non-GM commercial varieties. The identity of the test material was confirmed by PCR. The maize was introduced into the diets at approximately 33 % (weight/weight). Diets were formulated in accordance with the specifications of the Purina Mills Inc. Certified Rodent LabDiet® 5002.

During the study, all animals were observed daily for mortality and clinical signs, and detailed physical examinations were conducted weekly. Body weight and feed intake were recorded weekly. Prestudy and terminal (week 13) neurobehavioural and ophthalmological evaluations were conducted. In week 13, blood and urine samples were taken for coagulation, haematology, clinical chemistry and urinalysis. At necropsy, organs were weighed and gross pathology examination was carried out in all animals. Selected organs and tissues were preserved and histopathology was carried out on those from

[33] Dossier: Part II—Section A.3.5.
[34] Dossier: Part II—Section A.4.2.
[35] Additional information: 13/04/2015.
[36] Dossier: Part II—Section A.4.2.2 and additional information: 13/12/2013 and 20/04/2015.
[37] Dossier: Part II—Section A.4.3.
[38] Additional information: 05/12/2013 and 02/03/2015.

control and GM diet fed rats including all gross lesions. The EFSA GMO Panel noted that this 90-day study provided by the applicant exhibited some design weaknesses: only one dose level was tested and a limited number of organs and tissues were examined at histopathology (EFSA GMO Panel, 2011b).

No mortalities occurred in this study and there were no test material-related clinical signs.

Higher mean body weights and body weight gains, both statistically significant at most of the time points, were noted throughout the treatment period in females of the GM diet group compared with the control group. The difference in terminal body weight was approximately 8 %. No significant differences in feed intake were noted (except for during the first week).

Males given the GM maize showed a significantly lower mean serum cholesterol level and a significantly higher mean chloride level in comparison to the male control group. In females fed the GM maize mean serum alanine aminotransferase activity was significantly higher, while urea nitrogen was significantly lower in comparison to the female control group. These differences were not associated with changes in related parameters. In all cases, the mean values for GM-maize-fed animals were close to the mean values for the groups fed diets containing commercial varieties. Therefore, these findings are considered incidental.

No treatment-related macroscopic or microscopic findings were noted in organs or tissues. Sporadic findings are considered compatible with the spontaneous background pathology of rats of this strain and age.

Significant differences in some organ weights were noted between females fed the GM diet and those given the control diet: higher brain weight (absolute only), lower ovary/oviducts and thymus weight (both relative to body weight only), and lower thyroid/parathyroid weights (absolute only). In all cases the mean values were within or close to the means of the groups fed diets containing commercial maize varieties. In the absence of histopathological findings and/or changes in other related parameters, these organ weight differences are not considered toxicologically relevant.

No indications of adverse effects in the measured parameters were seen in this study. However, the EFSA GMO Panel notes that a 90-day feeding study in rodents on the whole GM food/feed was not necessary on the basis of preceding analyses.

3.3.1.4. Allergenicity

The strategies used to assess the potential risk of allergenicity focus on the source of the recombinant protein, on the potential of the newly expressed protein to induce sensitisation or to elicit allergic reactions in already sensitised persons, and on whether the transformation may have altered the allergenic properties of the modified plant.

Assessment of the allergenicity of the newly expressed protein[39]

A weight-of-evidence approach was followed, taking into account all of the information obtained on the newly expressed protein, since no single piece of information or experimental method yields sufficient evidence to predict allergenicity (Codex Alimentarius, 2009; EFSA GMO Panel, 2010c, 2011b).

The CP4 *epsps* gene originates from *Agrobacterium* sp. strain CP4, a soil microorganism that is not known to be allergenic.

Updated bioinformatic analyses of the amino acid sequences of the CP4 EPSPS protein, using the criterion of 35 % identity in a window of 80 amino acids, revealed no significant similarities to known allergens. In addition, the applicant also performed analyses searching for matches of eight contiguous

[39] Dossier: Part II—Section A.5; additional information: 20/04/2015.

identical amino acid sequences between the CP4 EPSPS protein and known allergens, which confirmed the outcome of the previous bioinformatic analysis.

The studies on the resistance of the CP4 EPSPS protein to degradation by proteolytic enzymes presented in the current application have been previously risk assessed by the EFSA GMO Panel (e.g. EFSA GMO Panel, 2012a, 2014).

The EFSA GMO Panel has previously evaluated the safety of the CP4 EPSPS protein in the context of several other applications and no concerns on allergenicity were identified (e.g. EFSA, 2006, 2008, 2009b, c; EFSA GMO Panel, 2011c, 2012a, b, 2013a, b, 2014). There is no information available on the structure or function of the newly expressed CP4 EPSPS protein that would suggest an adjuvant effect resulting in or increasing an eventual immunoglobulin E (IgE) response to a bystander protein.

The EFSA GMO Panel considers that there are no indications that the newly expressed CP4 EPSPS protein in maize MON 87427 may be allergenic.

Assessment of the allergenicity of the whole GM plant or crop[40]

To date, maize has not been considered to be a common allergenic food[41] (OECD, 2002), and, therefore, the EFSA GMO Panel did not request experimental data to analyse the allergen repertoire of GM maize. The EFSA GMO Panel regularly reviews the available publications on food allergy to maize (e.g. EFSA GMO Panel, 2013c).

In the context of the present application and considering the data from the molecular characterisation, the compositional analysis and the assessment of the newly expressed protein, the EFSA GMO Panel identified no indications of safety concern regarding the overall allergenicity of maize MON 87427.

3.3.1.5. Nutritional assessment of the genetically modified food/feed[42]

The intended trait of maize MON 87427 is herbicide tolerance, with no intention to alter the nutritional parameters. Comparison of the maize MON 87427 composition with its conventional counterpart did not identify differences that would require a safety assessment (see Section 3.2.1.4). Based on these data, the nutritional characteristics of maize MON 87427-derived food and feed are not expected to differ from those of conventional maize varieties.

3.3.1.6. Post-market monitoring of the genetically modified food/feed[43]

The EFSA GMO Panel considers that post-market monitoring of the GM food/feed is not necessary, given the absence of safety concerns identified for maize MON 87427.

3.3.2. Conclusions on the food/feed safety assessment

The safety assessment identified no concerns regarding the potential toxicity or allergenicity of the newly expressed CP4 EPSPS protein, and found no evidence that the genetic modification might significantly change the overall allergenicity of maize MON 87427. Based on the comparative analysis, the nutritional value of food and feed derived from maize MON 87427 is not expected to differ from that of food and feed derived from non-GM maize varieties. The EFSA GMO Panel concludes that maize MON 87427 assessed in this application is as safe and nutritious as its conventional counterpart and the commercial non-GM maize varieties tested. In addition, the EFSA GMO Panel found no indication that the introduction of the event MON 87427 into other maize varieties would affect its safety with respect to potential effects on human and animal health.

[40] Dossier: Part II—Section A.5.
[41] Directive 2007/68/EC of the European Parliament and of the Council of 27 November 2007 amending Annex IIIa to Directive 2000/13/EC of the European Parliament and of the Council as regards certain food ingredients. OJ L 310, 27.11.2007, p. 11–14.
[42] Dossier: Part II—Section A.6.
[43] Dossier: Part II—Section D.

3.4. Environmental risk assessment and monitoring plan

3.4.1. Evaluation of relevant scientific data

The scope of this application, EFSA-GMO-BE-2012-110, is for food and feed uses, import and processing, and does not include cultivation. Considering this scope of the maize MON 87427 application, the environmental risk assessment concerns the exposure of bacteria to recombinant DNA (i.e. in the gastrointestinal tract of animals fed GM material and those present in environments exposed to faecal material (manure and faeces) from animals fed maize MON 87427 grains (F_2 generation)) and the accidental release of viable grains of maize MON 87427 into the environment (i.e. during transportation and/or processing).

3.4.1.1. Environmental risk assessment

Potential unintended effects on plant fitness due to the genetic modification[44]

Maize is highly domesticated and generally unable to survive in the European environment without management intervention. Maize plants are not winter hardy in many regions of Europe, they have lost their ability to release seeds from the cob and they do not occur outside cultivated land or disturbed habitats in agricultural landscapes of Europe, despite cultivation for many years. In cultivation, maize volunteers may arise under some environmental conditions (mild winters). Observations of cobs, cob fragments or isolated grains shed in the field during harvesting indicate that grains may survive and overwinter in some regions, resulting in volunteers in subsequent crops. The occurrence of maize volunteers was reported in Spain and other European regions (e.g. Gruber et al., 2008). However, maize volunteers have been shown to grow weakly and flower asynchronously with the maize crop (Palaudelmàs et al., 2009).

The applicant presented agronomic and phenotypic data on maize MON 87427 (e.g. crop physiology, morphology, development and grain yield) gathered from eight field site locations in the USA during the 2010 growing season (see Section 3.2 for further details). The field trial data show statistically significant differences for five parameters (i.e. number of days to 50 % pollen shed, ear height, plant height, early stand count and grain moisture). Furthermore, for plant height, a significant genotype–environment interaction was identified, but no consistent relationship with descriptive site characteristics was observed (Section 3.2.1.3). Three of the five significant differences (number of days to 50 % pollen shed, ear height and plant height) were identified upon comparison of the conventional counterpart treated with conventional herbicides and maize MON 87427 treated with the same herbicide regime and the intended herbicide (glyphosate). The remaining two significant differences (early stand count and grain moisture) were identified only upon comparison of the conventional counterpart and maize MON 87427 when both were treated with conventional herbicides. The EFSA GMO Panel considers that, in the context of the scope of this application, the differences observed are unlikely to significantly affect the overall fitness, invasiveness or weediness of maize MON 87427. Therefore, the accidental release of maize MON 87427 grains (i.e. during transport and/or processing) would not result in the establishment of plants exhibiting dissemination capabilities different from existing conventional maize varieties, except for the tissue-specific expression of the CP4 EPSPS protein (for further details, see Section 3.2.1.3).

Seed[45] and pollen[46] characteristics of maize MON 87427 were also evaluated under growth chamber conditions (see Section 3.2 for further details). The studies show no significant differences in seed germination and pollen morphology between maize MON 87427 and its conventional counterpart (Section 3.2.1.3).

[44] Dossier: Part II—Section A.3.4, E3.1.
[45] Dossier: Part II—Section A.3.4,4.
[46] Dossier: Part II—Section A.3.4,5.

From the data presented in the application, there are no indications of an increased weed potential of maize MON 87427 compared with conventional maize. It can be considered that maize MON 87427 has no altered survival, multiplication or dissemination characteristics compared with its conventional counterpart.

In addition to the data presented by the applicant, the EFSA GMO Panel is not aware of any scientific report of increased spread and establishment of maize MON 87427 or maize with comparable properties, or of any change in survival capacity, including overwintering.

Survival of maize plants in the EU outside of cultivation or other areas is mainly limited by a combination of low competitiveness, absence of a dormancy phase, and susceptibility to plant pathogens, herbivores and cold climate conditions. Since these general characteristics are unchanged in maize MON 87427, the EFSA GMO Panel is of the opinion that the likelihood of unintended environmental effects due to the accidental release into the environment of viable grains from maize MON 87427 will not differ from that of conventional maize varieties.

Potential for gene transfer[47]

The EFSA GMO Panel evaluated the potential for horizontal and vertical gene flow for maize MON 87427, as well as the potential environmental consequences of such gene transfer. A prerequisite for any gene transfer is the availability of pathways for the transfer of genetic material, either through horizontal gene transfer of DNA or through vertical gene flow via the dispersal of pollen and seeds.

(a) Plant-to-bacteria gene transfer

Genomic plant DNA is a component of several food and feed products derived from maize. It is well documented that DNA present in food and feed becomes substantially degraded during processing and digestion in the human or animal gastrointestinal tract. However, a low level of exposure of fragments of ingested DNA, including the recombinant fraction of such DNA, to bacteria in the digestive tract of humans, domesticated animals and other environments exposed to the GM plant or plant material is expected.

Current scientific knowledge of recombination processes in bacteria indicates that horizontal transfer of non-mobile, chromosomally located DNA fragments between unrelated organisms (such as plants and bacteria) is not expected to occur at detectable frequencies under natural conditions (for further details, see EFSA, 2009a).

A successful horizontal gene transfer would require stable insertion of the recombinant DNA sequences into a bacterial genome and a selective advantage to be conferred on the transformed host. The only known mechanism to facilitate horizontal transfer of non-mobile, chromosomal DNA fragments to bacterial genomes is HR. In the case of sequence identity with the transgene itself, recombination would result in gene replacement.

A successful horizontal gene transfer would require stable insertion of the recombinant DNA sequences into a bacterial genome and a selective advantage to be conferred on the transformed host.

Bioinformatic analyses of the four regions of bacterial origin inserted into the genome of MON 87427 genes, i.e. the truncated left border, the CP4 EPSPS-coding sequence, the T-*nos* terminator and the right border of the insert, revealed that only two elements could provide sufficient length and sequence identity to facilitate HR with bacterial genomes. Since the sequence identity of those two elements which could facilitate HGT, i.e. the truncated left border and the T-*nos* terminator, are located on different plasmids (*A. tumefaciens* TiT37 octopine plasmid and *A. tumefaciens* Ti 15955 nopaline plasmid), the results of the bioinformatics analyses give no indication for facilitated double HR. Substitutive recombination of such elements with bacterial DNA would not confer any new trait on the

[47] Dossier: Part II—Sections A.2.2.2, E.3.1, E.3.2; additional information: 17/06/2013 and 20/04/2015.

recipient. Sequence identity with the modified CP4 *epsps* gene, which has been codon optimised for expression in plants, was not sufficient to facilitate HR-mediated transfer of the CP4 *epsps* gene from MON 87427 to bacteria[48].

In addition to homology-based recombination processes, non-homologous (illegitimate) recombination, which does not require similarity between the recombining DNA molecules, is theoretically possible. However, illegitimate recombination events have not been detected in studies that have exposed bacteria to high concentrations of GM plant DNA (see EFSA, 2009a). Thus, these processes are not considered to occur at levels that would make them relevant in assessments of plant-to-bacteria gene transfer events.

Because of the identity of the inserted DNA of bacterial origin in the genome of maize MON 87427, the EFSA GMO Panel concludes that the recombinant DNA in MON 87427 does not represent an environmental risk in relation to its potential for horizontal transfer to bacteria.

(b) Plant-to-plant gene transfer

Considering the scope of the maize MON 87427 application, which excludes cultivation, and the physical characteristics of maize seeds, the possible pathways for gene dispersal are through grain spillage and pollen of occasional feral GM maize plants originating from accidental grain spillage during transportation and/or processing.

The extent of cross-pollination of other maize varieties will mainly depend on the scale of accidental release during transportation and processing, and on the successful establishment and subsequent flowering of this GM maize plant. For maize, any vertical gene transfer is limited to other *Zea mays* plants, as populations of sexually compatible wild relatives of maize are not known in Europe (Eastham and Sweet, 2002; OECD, 2003).

The flowering of occasional feral GM maize plants, originating from accidental release occurring during transportation and processing, is unlikely to disperse significant amounts of GM maize pollen to other maize plants. Field observations performed on maize volunteers after GM maize cultivation in Spain revealed that maize volunteers had a low vigour, rarely had cobs and produced pollen that cross-pollinated neighbour plants at low levels (Palaudelmàs *et al.*, 2009).

Although the occurrence of some GM maize plants outside of cropped areas has been reported in Korea, as a result of grain spillage during import, transportation, storage, handling and processing (Kim et al., 2006; Lee et al., 2009; Park et al., 2010), survival of maize plants outside cultivation in Europe is mainly limited by a combination of low competitiveness, absence of a dormancy phase, and susceptibility to plant pathogens, herbivores and frost. As for any other maize varieties, GM maize plants would survive in subsequent seasons in only warmer regions of Europe and are not likely to establish feral populations under European environmental conditions.

The EFSA GMO Panel takes into account that this application does not include cultivation of maize MON 87427 within the EU; therefore, the likelihood of cross-pollination between cultivated maize and the occasional feral maize plants resulting from grain spillage is considered extremely low. However, in countries cultivating maize MON 87427 and producing seed for export, there is a potential for admixture and thus the introduction of GM seeds through this route.

In conclusion, as maize MON 87427 shows no detectable alterations in survival, multiplication or dissemination characteristics, the EFSA GMO Panel is of the opinion that the likelihood of unintended environmental effects as a consequence of spread of genes from this GM maize in Europe will not differ from that of conventional maize varieties.

Interactions of the GM plant with target organisms[49]

[48] Additional information: 17/06/2013.

Interactions of maize MON 87427 with target organisms are not considered an issue by the EFSA GMO Panel, as there are no target organisms.

Interactions of the GM plant with non-target organisms[50]

Owing to the scope of the maize MON 87427 application, which excludes cultivation, and the low level of exposure to the environment, potential interactions of the GM plant with non-target organisms are not considered an issue by the EFSA GMO Panel.

Interactions with the abiotic environment and biochemical cycles[51]

Because of the scope of the maize MON 87427 application, which excludes cultivation, and the low level of exposure to the environment, potential interactions with the abiotic environment and biogeochemical cycles are not considered an issue by the EFSA GMO Panel.

3.4.1.2. Post-market environmental monitoring[52]

The objectives of a PMEM plan, according to Annex VII of Directive 2001/18/EC, are (1) to confirm that any assumption regarding the occurrence and impact of potential adverse effects of the GMO, or its use, in the environmental risk assessment are correct; and (2) to identify the occurrence of adverse effects of the GMO, or its use, on human health or the environment that were not anticipated in the environmental risk assessment.

Monitoring is related to risk management, and thus a final adoption of the PMEM plan falls outside the mandate of EFSA. However, the EFSA GMO Panel gives its opinion on the scientific content of the PMEM plan provided by the applicant (EFSA GMO Panel, 2011a).

The potential exposure to the environment of maize MON 87427 would most likely be through faecal material from animals fed maize MON 87427 grains and/or through accidental release into the environment of GM maize grains (e.g. during transportation and/or processing). The scope of the PMEM plan provided by the applicant is in line with the intended uses. As the environmental risk assessment did not identify potential adverse environmental effects with regard to maize MON 87427, no case-specific monitoring is required.

The PMEM plan proposed by the applicant includes (1) the description of an approach involving operators (federations involved in maize import and processing) reporting to the applicant, via a centralised system, any observed adverse effect(s) of GMOs on human health and the environment; (2) a coordinating system established by EuropaBio for the collection of information recorded by the various operators; and (3) the use of networks of existing surveillance systems (Lecoq et al., 2007; Windels et al., 2008). The applicant proposes that a PMEM report is submitted on an annual basis.

The EFSA GMO Panel is of the opinion that the scope of the PMEM plan proposed by the applicant is in line with the intended uses of maize MON 87427, as the environmental risk assessment did not cover cultivation and identified no potential adverse environmental effects. The EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in its PMEM plan.

3.4.2. Conclusions on environmental risk assessment and monitoring plan

The scope of application EFSA-GMO-BE-2012-110 is for food and feed uses, import and processing, and does not include cultivation. Considering the scope of this maize MON 87427 application, the environmental risk assessment is concerned with indirect exposure, mainly through faecal material

[49] Dossier: Part II—Section E.3.3.
[50] Dossier: Part II—Section E.3.4.
[51] Dossier: Part II—Section E.3.6.
[52] Dossier: Part II—Section E.4.

from animals fed grains from maize MON 87427, and with the accidental release into the environment of viable maize MON 87427 (e.g. during transportation and/or processing).

In the case of accidental release into the environment of viable seeds of maize MON 87427, there are no indications of an increased likelihood of spread and establishment of feral maize MON 87427 plants. Considering its intended use for food and feed, environmental risks associated with an unlikely, but theoretically possible, horizontal gene transfer from maize MON 87427 to bacteria have not been identified. Potential interactions of maize MON 87427 with the biotic and abiotic environment were not considered, because of the scope of the GM maize application and hence the low level of exposure. The scope of the PMEM plan provided by the applicant and the proposed reporting intervals are in line with the intended uses of maize MON 87427 and the guidance document of the EFSA GMO Panel on PMEM of GM plants (EFSA GMO Panel, 2011a). The EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in its PMEM plan.

4. Conclusions

The EFSA GMO Panel was asked to carry out a scientific assessment of maize MON 87427 for import, processing, and food and feed uses in accordance with Regulation (EC) No 1829/2003.

The molecular characterisation data provided for maize MON 87427 did not give rise to safety issues.

The EFSA GMO Panel concluded that none of the differences identified in the composition, agronomic and phenotypic characteristics of grain and forage obtained from maize MON 87427 required further assessment regarding food and feed safety. No concerns regarding the potential toxicity or allergenicity of the newly expressed CP4 EPSPS protein were identified, and no evidence that the genetic modification might significantly change the overall allergenicity of maize MON 87427 was found. The nutritional value of food and feed derived from maize MON 87427 is not expected to differ from that of food and feed derived from non-GM maize varieties. The EFSA GMO Panel concludes that maize MON 87427, assessed in this application, is as safe and nutritious as its conventional counterpart and the non-GM maize reference varieties tested. In addition, the EFSA GMO Panel found no indication that the introduction of the event MON 87427 into other maize varieties would affect safety with respect to potential effects on human and animal health.

Considering the scope of the maize MON 87427 application, which excludes cultivation, there is no requirement for a scientific assessment of possible environmental effects associated with the cultivation of this GM maize. The EFSA GMO Panel concluded that there is a very low likelihood of environmental effects resulting from the accidental release of viable grains from maize MON 87427 into the environment.

Considering the scope of the application with regard to food and feed use, interactions with the biotic and abiotic environment were not considered an issue. Risks associated with an unlikely, but theoretically possible, horizontal gene transfer from maize MON 87427 to bacteria have not been identified. The scope of the PMEM plan provided by the applicant is in line with the intended uses of maize MON 87427 and the guidance document of the EFSA GMO Panel on PMEM of GM plants (EFSA, 2011a). The EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in the monitoring plan.

In conclusion, the EFSA Panel on Genetically Modified Organisms considers that the information available for maize MON 87427 addresses the scientific comments raised by Member States and that the maize MON 87427, as described in this application, is as safe as its conventional counterpart and non-GM reference varieties with respect to potential effects on human and animal health and the environment in the context of the scope of the application.

DOCUMENTATION AS PROVIDED TO EFSA

1. Letter from the Competent Authority of Belgium, received on 21 June 2012, concerning a request for the placing on the market of genetically modified maize MON 87427 submitted by Monsanto Europe S.A./N.V. in accordance with Regulation (EC) No 1829/2003 (application reference EFSA-GMO-BE-2012-110).

2. Acknowledgement of receipt letter, dated 17 July 2012, from EFSA to the Competent Authority of Belgium.

3. Letter from EFSA to the applicant, dated 12 September 2012, requesting additional information under completeness check.

4. Letter from the applicant to EFSA, received on 9 October 2012, providing additional information under completeness check.

5. Letter from EFSA to the applicant, dated 30 October 2012, requesting additional information under completeness check.

6. Letter from the applicant to EFSA, received on 28 November 2012, providing additional information under completeness check.

7. Letter from EFSA to the applicant, dated 3 January 2013, delivering the "Statement of Validity" of the application for the placing on the market of genetically modified maize MON 87427 (EFSA-GMO-BE-2012-110), submitted in accordance with Regulation (EC) No 1829/2003 by Monsanto Europe S.A./N.V.

8. Letter from EFSA to the applicant, dated 11 April 2013, requesting additional information and stopping the clock.

9. Letter from the applicant to EFSA, received on 22 May 2013, providing the timeline for submission of responses.

10. Letter from EFSA to the applicant, dated 3 June 2013, requesting additional information and maintaining the clock stopped.

11. Letter from the applicant to EFSA, received on 17 June 2013, providing the additional information requested on 11 April 2013.

12. Letter from the applicant to EFSA, received on 17 June 2013, providing the additional information requested on 3 June 2013.

13. Letter from EFSA to the applicant, dated 13 August 2013, requesting additional information and maintaining the clock stopped.

14. Letter from the applicant to EFSA, received on 28 August 2013, providing the timeline for submission of responses.

15. Letter from the applicant to EFSA, received on 11 September 2013, providing additional information.

16. Letter from the applicant to EFSA, received on 5 December 2013, providing additional information spontaneously.

17. Letter from the applicant to EFSA, received on 13 December 2013, providing additional information spontaneously.

18. Letter from the applicant to EFSA, received on 21 March 2014, requesting clarifications.

19. Letter from EFSA to the applicant, dated 8 May 2014, providing clarifications.

20. Letter from EFSA to the applicant, dated 6 June 2014, requesting additional information and maintaining the clock stopped.

21. Letter from the applicant to EFSA received on 8 July 2014 providing additional information.

22. Letter from EFSA to the applicant, dated 19 November 2014, re-starting the clock.

23. Letter from EFSA to the applicant, dated 15 December 2014, requesting additional information and stopping the clock.

24. Letter from the applicant to EFSA, received 28 January 2015, providing the timeline for submission of responses.

25. Letter from the applicant to EFSA, received on 2 March 2015, providing additional information.

26. Letter from EFSA to the applicant, dated 16 March 2015, requesting additional information and maintaining the clock stopped.

27. Letter from the applicant to EFSA, received on 13 April 2015, providing additional information.

28. Letter from the applicant to EFSA, received on 20 April 2015, providing additional information.

29. Letter from EFSA to the applicant, dated 7 May 2015, requesting additional information and maintaining the clock stopped.

30. Letter from the applicant to EFSA, received on 8 May 2015, providing additional information.

31. Letter from EFSA to the applicant, dated 26 May 2015, re-starting the clock.

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